VERIFICATION OF A TRANSLATION

Re: U.S. Patent Application Serial No. **10/520,282** filed on **February 22, 2006**.

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hereby declare that I am the translator of the document attached, Japanese Patent Application No. 2002-244374, filed August 23, 2002, and certify that the following is a true translation to the best of my knowledge and belief.

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Haruhito OHISIHI

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【Applicant】

【ID Number】 000229117

【Name of Document】 DESCRIPTION

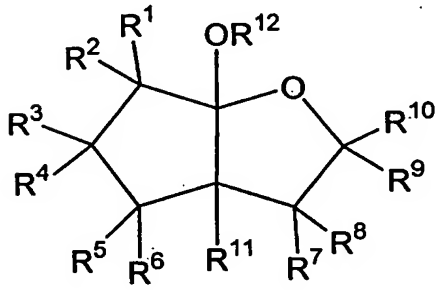
【Name of the Invention】 2-OXABICYCLO[3.3.0]OCTANE COMPOUNDS, PROCESS FOR PRODUCING THE SAME, AND OPTICAL RESOLVER

【Claims】

【Claim 1】

A 2-oxabicyclo[3.3.0]octane compound of the following formula (1),

【Chemical formula 1】



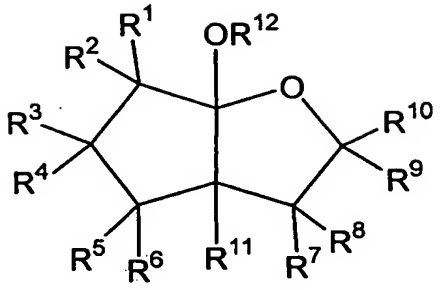
(1)

wherein R^1-R^{10} individually represent a hydrogen atom or a substituted or unsubstituted alkyl group having 1-20 carbon atoms, R^{11} represents a hydrogen atom, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkynyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkenyl group, a substituted or unsubstituted aryl group, formyl group, a substituted or unsubstituted acyl group, a substituted or unsubstituted alkoxycarbonyl group, a substituted or unsubstituted alkenyloxycarbonyl group, or a substituted or unsubstituted aryloxycarbonyl group, and R^{12} represents a substituted or unsubstituted hydrocarbon group.

【Claim 2】

A process for producing a 2-oxabicyclo[3.3.0]octane compound represented by the above formula (1),

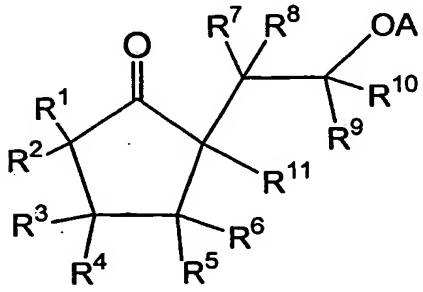
【Chemical formula 3】



(1)

(wherein R^1-R^{12} are the same as defined above) comprising reacting a cyclopentanone compound of the formula (2),

【Chemical formula 2】



(2)

wherein the R^1-R^{11} groups are the same as in the formula (1) and A is a protective group for a hydroxyl group, with an alcohol of the formula $R^{12}OH$, wherein R^{12} is the same as in the formula (1), in the presence of an acid catalyst.

【Claim 3】

An optical resolution agent comprising at least one 2-oxabicyclo[3.3.0]octane compound of the formula (1) as described above.

【Detailed Description of the Invention】

【0001】

【Technical field to which the Invention pertains】

The present invention provides a compound having a 2-oxabicyclo[3.3.0]octane skeleton with a hydrocarbon group bonded to position 1 via an oxygen atom and a

substituent selected from various groups such as hydrogen, alkoxycarbonyl, and the like bonded to position 5 (hereinafter referred to as 2-oxabicyclo[3.3.0]octane compound), a process for producing the compound, and an optical resolving agent.

【0002】

【Description of the Prior Art】

Many physiologically active substances such as pharmaceuticals, agricultural chemicals, perfumes, and sweeteners are alcohols having an asymmetric carbon atom. There may be optical isomers in such a compound. However, there may be a significant difference in the degree of physiological activity among these optical isomers. Some isomers exhibit physiological activity quite different from others. Therefore, development of a method for separating an optical isomer mixture of alcohols or compounds having a partial structure of such an alcohol (hereinafter referred to simply as "alcohols") easily without failure has been desired.

【0003】

As an example of optically resolving an alcohol, Synlett., (6), 862 (2000), J. Org. Chem., 64, 2638 (1999), and the like describe a method comprising allowing one of optical isomers to remain as the alcohol and transforming the other optical isomer into an ester derivative in a natural optically active environment (for example, internal organs of animals containing an esterified enzyme or hydrolyzed enzyme). However, since such an enzyme does not have chemical stability, in particular, thermal stability, the enzyme cannot be used under high temperature conditions. Further, it is difficult for the enzyme to be generally and widely accepted due to its high cost and difficulty in being procured in a large amount.

【0004】

Tetrahedron., Lett., 35, 4397 (1994) reported an experiment in which an ester prepared by condensing a carboxylic acid having an asymmetric carbon atom with an alcohol was separated into individual diastereomers by silica gel column chromatography.

In principle, this is optical resolution of an alcohol.

However, since there are no general rules or principles for producing a highly separable diastereomer mixture, the method cannot be generally applied.

【0005】

And the mixture can rarely be separated into two optical isomers without being influenced by an external optically active factor, such as in the case of spontaneous resolution. General rules for separation do not exist. Accordingly, in almost all cases, it is highly difficult to speculate whether or not an optical isomer mixture of alcohol and the like can be separated into optically active compounds. The mixture is not easily separated in almost all cases.

【0006】

【Problems to be solved by the invention】

The present invention has been achieved in view of this situation and has an objective of providing a novel 2-oxabicyclo[3.3.0]octane compound which can be used as an optical resolving agent of an optical isomer mixture such as alcohol, a process for producing the same, and an optical resolving agent containing at least one 2-oxabicyclo[3.3.0]octane compound.

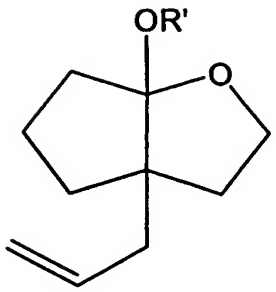
【0007】

【Means for Solving the Problem】

The present inventors previously reported that 1-alkoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane and the like represented by the formula (A) can be used as an optical resolution agent of an optical isomer mixture such as alcohol (WO02/072505 (PCT/JP02/01644)).

【0008】

【Chemical formula 4】



(A)

【0009】

wherein R' represents a methyl group or the like.

【0010】

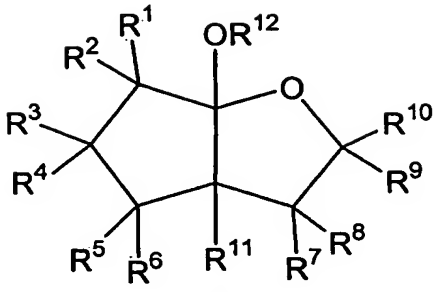
The present inventors have conducted extensive studies to obtain a 2-oxabicyclo[3.3.0]octane compound which has various substituents at position 5 of the 2-oxabicyclo[3.3.0]octane ring as an analogue of the compound represented by the formula (A). As a result, the present inventors have found that a 2-oxabicyclo[3.3.0]octane compound which has a hydrogen atom, an alkoxycarbonyl group, or the like bonded to position 5 of the 2-oxabicyclo[3.3.0]octane ring can be prepared efficiently by a reaction of a cyclopentanone compound having a 2-acetoxyethyl group and a substituent such as a hydrogen atom or an alkoxycarbonyl group at position 2 of a cyclopentanone ring, with an alcohol in the presence of an acid catalyst, and that this compound can be used as an optical resolving agent for an optical isomer mixture such as alcohol. These findings led to the completion of the present invention.

【0011】

The present invention thus provides a 2-oxabicyclo [3.3.0]octane compound of the formula (1),

【0012】

【Chemical formula 5】



(1)

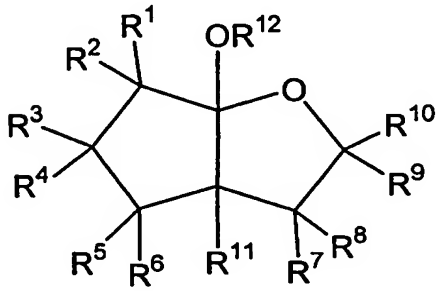
【0013】

wherein R^1-R^{10} individually represent a hydrogen atom or a substituted or unsubstituted alkyl group having 1-20 carbon atoms, R^{11} represents a hydrogen atom, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkynyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkenyl group, a substituted or unsubstituted aryl group, formyl group, a substituted or unsubstituted acyl group, a substituted or unsubstituted alkoxycarbonyl group, a substituted or unsubstituted alkenyloxycarbonyl group, or a substituted or unsubstituted aryloxycarbonyl group, and R^{12} represents a substituted or unsubstituted hydrocarbon group.

The present invention further provides a process for producing a 2-oxabicyclo[3.3.0]octane compound represented by the above formula (1),

【0015】

【Chemical formula 7】



(1)

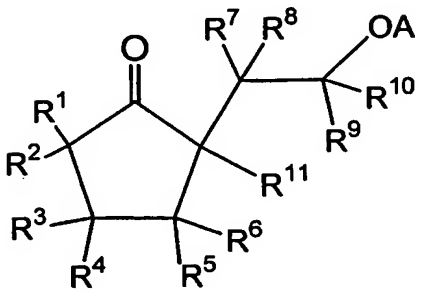
【0016】

(wherein R^1-R^{12} are the same as defined above) comprising reacting a

cyclopentanone compound of the formula (2),

【0014】

【Chemical fomula 6】



(2)

wherein the R^1-R^{11} groups are the same as in the formula (1) and A represents a protective group for a hydroxyl group, with an alcohol of the formula $R^{12}OH$, wherein R^{12} is the same as in the formula (1).

【0017】

The present invention further provides an optical resolution agent comprising at least one 2-oxabicyclo [3.3.0]octane compound of the formula (1).

【0018】

【Preferred Embodiment of the Invention】

The present invention will be described in detail in the following sections.

(1) 2-oxabicyclo[3.3.0]octane compound

In the first place, the present invention provides a 2-oxabicyclo [3.3.0]octane compound of the above formula (1).

In the above formula (1), R^1-R^{10} individually represent a hydrogen atom or a substituted or unsubstituted alkyl group having 1-20 carbon atoms.

Examples of the alkyl group having 1-20 carbon atoms include a methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, sec-butyl group, isobutyl group, n-pentyl group, n-hexyl group, n-octyl group, n-nonyl group, and n-decyl group. Examples of the substituent for these groups include a hydroxyl group; alkoxy groups

such as a methoxy group and ethoxy group; alkylthio groups such as a methylthio group and ethylthio group; halogen atoms such as a fluorine atom and chlorine atom; and substituted or unsubstituted phenyl groups such as a phenyl group, 2-chlorophenyl group, 3-methoxyphenyl group, and 4-methylphenyl group. Of these, a compound in which R^1-R^{10} are individually a hydrogen atom or a methyl group is preferable, since the compound can be easily made available or produced. A compound in which all R^1-R^{10} groups are a hydrogen atom is particularly preferable.

【0019】

R^{11} represents a hydrogen atom, a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkynyl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkenyl group, a substituted or unsubstituted aryl group, formyl group, a substituted or unsubstituted acyl group, a substituted or unsubstituted alkoxycarbonyl group, a substituted or unsubstituted alkenyloxycarbonyl group, or a substituted or unsubstituted aryloxycarbonyl group.

【0020】

Examples of the alkyl group include a methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, sec-butyl group, t-butyl group, n-pentyl group, and n-hexyl group.

As examples of the alkynyl group, an ethynyl group, propargyl group, and 1-butynyl group can be given.

Examples of the cycloalkyl group include a cyclopropyl group, cyclopentyl group, cyclohexyl group, and cyclooctyl group.

Examples of the cycloalkenyl group include a cyclopentenyl group, cyclohexenyl group, and cyclooctenyl group.

Examples of the aryl group include a phenyl group, 1-naphthyl group, and 2-naphthyl group.

【0021】

There are no specific limitations to the substituents of the alkyl group, alkynyl group, cycloalkyl group, cycloalkenyl group, and aryl group inasmuch as the substituents are stable in an acid. As examples, an alkoxy group, alkoxycarbonyl group, hydroxyl group, acyl group, nitro group, cyano group, halogen atom, phenyl group, and heterocyclic group can be given. There are no specific limitations to the position for these substituents. Two or more substituents, either the same or different, may bond with a hydrocarbon group.

【0022】

Examples of the substituted or unsubstituted acyl group include an acetyl group, propionyl group, butyryl group, benzoyl group, 4-methylbenzoyl group, and 2,4,6-trimethylbenzoyl group.

【0023】

Examples of the alkoxycarbonyl group include a methoxycarbonyl group, ethoxycarbonyl group, n-propoxycarbonyl group, isopropoxycarbonyl group, n-butoxycarbonyl group, sec-butoxycarbonyl group, tert-butoxycarbonyl group, n-pentyloxycarbonyl group, and n-hexyloxycarbonyl group.

【0024】

Examples of the alkenyloxycarbonyl group include a vinyloxycarbonyl group, 1-propenyloxycarbonyl group, 2-propenyloxycarbonyl group, isopropenyloxycarbonyl group, 2-butenyloxycarbonyl group, methallyloxycarbonyl group, 2-pentenyloxycarbonyl group, and 2-hexenyloxycarbonyl group.

Examples of the aryloxycarbonyl group include a phenoxycarbonyl group, 1-naphthyloxycarbonyl group, and 2-naphthyloxycarbonyl group.

【0025】

As examples of the substituents for the alkoxycarbonyl group, alkenyloxycarbonyl group, and aryloxycarbonyl group, a halogen atom, alkoxy group, alkylthio group, alkylsulfonyl group, cyano group, nitro group, substituted or

unsubstituted phenyl group, and substituted or unsubstituted heterocyclic group can be given. There are no specific limitations to the positions of these substituents. Two or more substituents, either the same or different, may bond to one group.

【0026】

Of these, for the reasons of easy availability and easy manufacturing, R^{11} is preferably a hydrogen atom, substituted or unsubstituted alkyl group, substituted or unsubstituted alkoxycarbonyl group, substituted or unsubstituted alkenyloxycarbonyl group, or substituted or unsubstituted aryloxycarbonyl group, more preferably a hydrogen atom, substituted or unsubstituted alkyl group, or substituted or unsubstituted alkoxycarbonyl group, and particularly preferably a hydrogen atom, or substituted or unsubstituted alkoxycarbonyl group. And the number of carbon atoms in R^{11} is preferably 1 to 20.

【0027】

R^{12} represents a substituted or unsubstituted hydrocarbon group, preferably a substituted or unsubstituted hydrocarbon group having 1-20 carbon atoms. The hydrocarbon group may be a primary, secondary, or tertiary hydrocarbon group, and may be or may not be a group having an asymmetric carbon atom. In case that the hydrocarbon group represented by R^{12} has an asymmetric carbon atom in the molecule, R^{12} may be a chiral (optical active) group or may be an optical isomer mixture.

【0028】

As the hydrocarbon group represented by R^{12}, an alkyl group, alkenyl group, alkynyl group, cycloalkyl group, cycloalkenyl group, and hydrocarbon group having a bridged structure can be given.

【0029】

As examples of the alkyl group represented by R^{12}, a methyl group, ethyl group, n-propyl group, isopropyl group, n-butyl group, isobutyl group, sec-butyl group, t-butyl group, n-pentyl group, isopentyl group, neopentyl group, n-hexyl group, isohexyl group,

n-heptyl group, n-octyl group, n-nonyl group, n-decyl group, n-undecyl group, and n-dodecyl group can be given. As examples of the alkenyl group, 1-propenyl group, 2-propenyl group, 1-butenyl group, 2-butenyl group, 3-butenyl group, 1-pentenyl group, 2-pentenyl group, 3-pentenyl group, 4-pentenyl group, 1-hexenyl group, 2-hexenyl group, 3-hexenyl group, 4-hexenyl group, 5-hexenyl group, 1-heptenyl group, 2-heptenyl group, 5-heptenyl group, 6-heptenyl group, 1-octenyl group, 2-octenyl group, 4-octenyl group, and 7-octenyl group can be given.

【0030】

As examples of the alkynyl group, a 1-propynyl group, 2- propynyl group, 1-butynyl group, 2- butynyl group, 3-butynyl group, 1-pentynyl group, 2-pentynyl group, 4-pentynyl group, 1-hexynyl group, 2-hexynyl group, 5-hexynyl group, 1-heptynyl group, 2-heptynyl group, 4-heptynyl group, 6-heptynyl group, and 1-octynyl group can be given.

Examples of the cycloalkyl group include cycloalkyl groups such as a cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, and cyclooctyl group.

【0031】

Examples of the cycloalkenyl group include cycloalkenyl groups such as 2-cyclopentenyl group, 3-cyclopentenyl group, 2-cyclohexenyl group, 3-cyclohexenyl group, 2-cycloheptenyl group, and 3-cyclooctenyl group. As examples of the hydrocarbon group having a bridged structure, bicyclo[2.1.0]pentyl group, bicyclo[4.1.0]heptan-3-yl group, bicyclo[2.2.1]heptan-2-yl group, and bicyclo[3.2.1]octan-6-yl group can be given.

【0032】

As examples of the substituent for the hydrocarbon group represented by R^{12}, a haloalkyl group, alkoxy group, alkoxycarbonyl group, alkylthio group, alkylsulfonyl group, acyl group, acylamino group, nitro group, cyano group, halogen atom, silyl group, substituted or unsubstituted phenyl group, and substituted or unsubstituted heterocyclic

group can be given.

There are no specific limitations to the positions of these substituents. Two or more substituents, either the same or different, may bond to the hydrocarbon group.

【0033】

Specific examples of the 2-oxabicyclo[3.3.0]octane compound represented by the formula (1) include:

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a hydrogen atom such as 1-methoxy-2-oxabicyclo[3.3.0]octane, 1-ethoxy-2-oxabicyclo[3.3.0]octane, 1-sec-butoxy-2-oxabicyclo[3.3.0]octane, 1-(1-methyloctyloxy)-2-oxabicyclo[3.3.0]octane, 1-(1-trifluoromethylpropoxy)-2-oxabicyclo[3.3.0]octane, 1-(d)-bornyloxy-2-oxabicyclo[3.3.0]octane, 1-(1)-bornyloxy-2-oxabicyclo[3.3.0]octane, 1-(1-(S)-ethoxycarbonyl)ethoxy-2-oxabicyclo[3.3.0]octane, 1-(1-(R)-ethoxycarbonyl)ethoxy-2-oxabicyclo[3.3.0]octane, 1-(1)-mentyloxy-2-oxabicyclo[3.3.0]octane, and 1-(d)-menthyloxy-2-oxabicyclo[3.3.0]octane;

【0034】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted alkyl group such as 1-methoxy-5-methyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-ethyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-n-propyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-isopropyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-n-butyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-tert-butyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-n-pentyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-n-hexyl-2-oxabicyclo[3.3.0]octane, 1-methoxy-5-benzyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(2-phenylethyl)-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-methoxymethyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-methylthiomethyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-methylsulfonyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-cyanomethyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-chloromethyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-trimethylsilylmethyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-methoxycarbonylmethyl-2-oxabicyclo[3.3.0]octane,

【0035】

1-ethoxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-sec-butoxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(1-methyloctyloxy)-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(1-trifluoromethyl-n-propoxy)-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(d)-bornyloxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(1)-bornyloxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(1-(S)-ethoxycarbonyl)ethoxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(1-(R)-ethoxycarbonyl)ethoxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(1)-mentyloxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-(d)-mentyloxy-5-methyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-diphenylmethyl-2-oxabicyclo[3.3.0]octane,

1-ethoxy-5-diphenylmethyl-2-oxabicyclo[3.3.0]octane,

【0036】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted cycloalkyl group such as 1-methoxy-5-cyclopropyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-cyclohexyl-2-oxabicyclo[3.3.0]octane,

1-ethoxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-sec-butoxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-(1-methyloctyloxy)-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-(1-trifluoromethylpropoxy)-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-(d)-bornyloxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-(l)-bornyloxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-(1-(S)-ethoxycarbonyl)ethoxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-(1-(R)-ethoxycarbonyl)ethoxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane,

1-(l)-mentyloxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane, and

1-(d)-mentyloxy-5-cyclopentyl-2-oxabicyclo[3.3.0]octane;

【0037】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted cycloalkenyl group such as 1-methoxy-5-cyclopentenyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane,

1-ethoxy-5-cyclopentenyl-2-oxabicyclo[3.3.0]octane,

1-sec-butoxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane,

1-(1-methyloctyloxy)-5-cyclopentenyl-2-oxabicyclo[3.3.0]octane,

1-(1-trifluoromethylpropoxy)-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane,

1-(d)-bornyloxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane,

1-(l)-bornyloxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane,

1-(1-(S)-ethoxycarbonyl)ethoxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane,

1-(1-(R)-ethoxycarbonyl)ethoxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane,

1-(l)-mentyloxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane, and

1-(d)-mentyloxy-5-cyclohexenyl-2-oxabicyclo[3.3.0]octane;

【0038】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted alkynyl group such as 1-methoxy-5-ethynyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-ethoxy-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-sec-butoxy-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-(1-methyloctyloxy)-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-(1-trifluoromethylpropoxy)-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-(d)-bornyloxy-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-(1)-bornyloxy-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-(1-(S)-ethoxycarbonyl)ethoxy-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-(1-(R)-ethoxycarbonyl)ethoxy-5-propargyl-2-oxabicyclo[3.3.0]octane,

1-(1)-mentyloxy-5-propargyl-2-oxabicyclo[3.3.0]octane, and

1-(d)-mentyloxy-5-propargyl-2-oxabicyclo[3.3.0]octane;

【0039】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted aryl group such as 1-methoxy-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(4-methylphenyl)-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(4-chlorophenyl)-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(2,4,6-trimethylphenyl) -2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(1-naphthyl)-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(2-naphthyl)-2-oxabicyclo[3.3.0]octane,

1-ethoxy-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-sec-butoxy-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-(1'-methyloctyloxy)-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-(1-trifluoromethylpropoxy)-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-(d)-bornyloxy-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-(1)-bornyloxy-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-(1-(S)-ethoxycarbonyl)ethoxy-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-(1-(R)-ethoxycarbonyl)ethoxy-5-phenyl-2-oxabicyclo[3.3.0]octane,

1-(1)-mentyloxy-5-phenyl-2-oxabicyclo[3.3.0]octane, and

1-(d)-mentyloxy-5-phenyl-2-oxabicyclo[3.3.0]octane;

【0040】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a formyl group or a substituted or unsubstituted acyl group such as 1-methoxy-5-formyl-2-oxabicyclo[3.3.0]octane,
1-methoxy-5-acetyl-2-oxabicyclo[3.3.0]octane,
1-methoxy-5-propionyl-2-oxabicyclo[3.3.0]octane,
1-methoxy-5-benzoyl-2-oxabicyclo[3.3.0]octane, and
1-methoxy-5-(4-methylbenzoyl)-2-oxabicyclo[3.3.0]octane;

【0041】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted alkoxycarbonyl group such as 1-methoxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-methoxy-5-ethoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-ethoxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-sec-butoxy-5-ethoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-(1-methyloctyloxy)-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-(1-trifluoromethylpropoxy)-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-(1-(S)-ethoxycarbonyl)ethoxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-(1-(R)-ethoxycarbonyl)ethoxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-(1)-mentyloxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-(d)-mentyloxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane,
1-(d)-bornyloxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane, and
1-(1)-bornyloxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane;

【0042】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted alkenyloxycarbonyl group such as
1-methoxy-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane,
1-methoxy-5-isopropenyloxycarbonyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-methallyloxycarbonyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-cinnamyloxycarbonyl-2-oxabicyclo[3.3.0]octane,

1-(1-methyloctyloxy)-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane,

1-(1-trifluoromethylpropoxy)-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane,

1-(d)-bornyloxy-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane,

1-(l)-bornyloxy-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane,

1-(1-(S)-ethoxycarbonyl)ethoxy-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane,

1-(1-(R)-ethoxycarbonyl)ethoxy-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane,

1-(l)-menthyloxy-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane, and

1-(d)-menthyloxy-5-(2-propenyloxy)carbonyl-2-oxabicyclo[3.3.0]octane;

【0043】

2-oxabicyclo[3.3.0]octane compounds in which R^{11} is a substituted or unsubstituted aryloxycarbonyl group such as

1-methoxy-5-phenoxycarbonyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(4-methylphenoxy)carbonyl-2-oxabicyclo[3.3.0]octane,

1-methoxy-5-(1-naphthyloxycarbonyl)-2-oxabicyclo[3.3.0]octane, and

1-methoxy-5-(2-naphthyloxycarbonyl)-2-oxabicyclo[3.3.0]octane.

【0044】

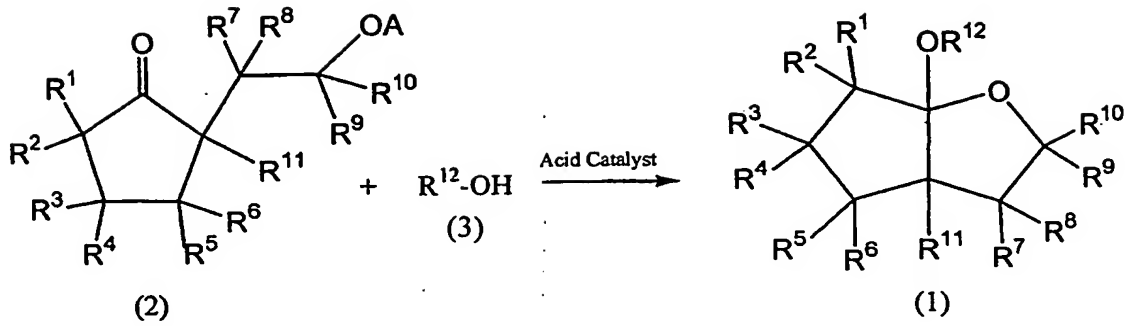
(2) Process for producing 2-oxabicyclo[3.3.0]octane compound

In the second place, the present invention provides a process for producing 2-oxabicyclo[3.3.0]octane compound of the above formula (1).

The 2-oxabicyclo[3.3.0]octane compound (1) can be produced by the following process.

【0045】

【Chemical Formula 8】



(2) (1)

【0046】

The 2-oxabicyclo[3.3.0]octane compound (1) can be prepared by reacting a cyclopentanone compound of the formula (2) with an alcohol of the formula (3) (hereinafter referred to as " alcohol(3)") in the presence of an acid catalyst.

【0047】

In the formulae, R^1-R^{12} are the same as defined above and A indicates a protective group of the hydroxyl group. As examples of the group A, a formyl group, acetyl group, propionyl group, benzoyl group, 4-chlorobenzoyl group, tert-butoxy carbonyl group, 2-tetrahydrofuranyl group, 2-tetrahydropyranyl group, 1-ethoxyethyl group, 1-ethoxyethoxy group, and tert-butyl can be given. Of these, due to easy availability and capability of producing the target compound at a high yield, an acetyl group and benzoyl group are preferable, with an acetyl group being particularly preferable.

【0048】

The alcohol (3) usually has 1-20 carbon atoms, may be a primary, secondary, or tertiary alcohol, and either may have or may not have an asymmetric carbon atom in the molecule. In case that alcohol (3) has an asymmetric carbon atom in the molecule, the alcohol(3) may be an optically active alcohol or may be a mixture of optical isomers.

Although there are no specific limitations to the amount of the alcohol (3), the alcohol (3) is usually used in an amount of 1-100 mols, and preferably 1-5 mols, for 1 mol of the cyclopentanone compound (2).

【0049】

The reaction can be carried out by stirring a mixture of the cyclopentanone compound (2) and the alcohol (3) in a suitable solvent or without using a solvent in the presence of an acid catalyst.

As the acid catalyst, either a liquid acid catalyst or a solid acid catalyst can be used without any specific limitations. For example, pyridinium p-toluenesulfonate (PPTS), p-toluenesulfonic acid (p-TsOH), montmorillonite, an acidic ion exchange resin, and synthetic zeolite (e.g. molecular sieve) can be given.

The acid catalyst is usually used in the amount of usually 0.0001-2 parts by weight, and preferably 0.001-1 part by weight, for 1 part by weight of the cyclopentanone compound (2).

【0050】

There are no specific limitations to the solvent used for the reaction inasmuch as the solvent is an inert solvent. The solvent is preferably nonprotonic. Examples of the solvent include aromatic hydrocarbons such as benzene, toluene, xylene, and chlorobenzene, dichlorobenzene; aliphatic hydrocarbons such as n-pentane, n-hexane, n-heptane, n-octane, cyclohexane, methylcyclohexane, and petroleum ether; esters such as ethyl acetate, n-propyl acetate, and n-butyl acetate; halogenated hydrocarbons such as dichloromethane, chloroform, carbon tetrachloride, and 1,2-dichloroethane; ethers such as diethyl ether, dibutyl ether, diisobutyl ether, tetrahydrofuran, 1,4-dioxane, 1,2-dimethoxyethane, cyclopentyl methyl ether, and anisole; and amides such as N,N-dimethylformamide, N,N-dimethylacetamide, and N-methylpyrrolidone. These solvents may be used either individually or in combination of two or more. Of these, an organic solvents having a comparatively low boiling point such as aromatic hydrocarbons, aliphatic hydrocarbons, and halogenated hydrocarbons are preferably used.

【0051】

The reaction is smoothly carried out in the temperature range of –20°C to the boiling point of the solvent used, and more preferably in the temperature range of –10°C

to 150°C. The reaction is completed usually in several minutes to several ten hours.

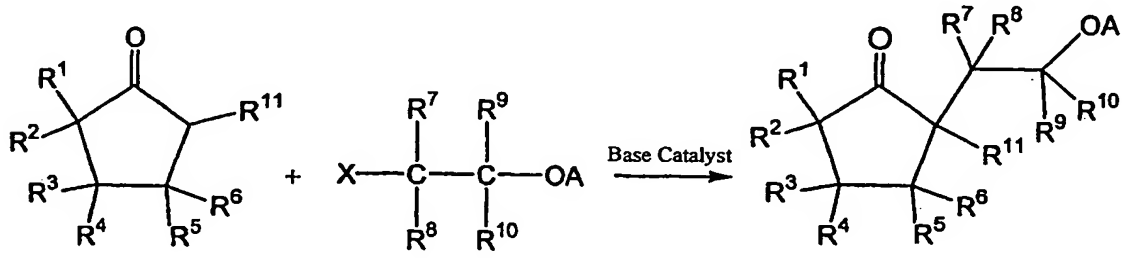
【0052】

The cyclopentanone compound (2) used as the raw material can be produced according to the method described in Tetrahedron Lett., 35, 7785 (1994), for example.

A common production route is shown as follows.

【0053】

【Chemical formula 9】



(4) (5) (2)

【0054】

In the formulae, R^1 to R^{11} and A respectively represent the same groups as defined above and X represents a halogen atom such as chlorine, bromine, or iodine.

Specifically, the cyclopentanone compound (2) can be obtained by reacting a cyclopentanone compound of the formula (4) with a halogenated alkyl of the formula (5) in the presence of a base catalyst.

【0055】

After the reaction and a common post treatment, the targeted 2-oxabicyclo[3.3.0]octane compound (1) can be obtained by known separating means such as column chromatography, a simulated moving bed chromatography, distillation, and the like.

【0056】

Among the compounds of the formula (1), the compound in which R^{11} is a substituted or unsubstituted alkyl group can also be obtained from a compound in which

R^{11} is a substituted or unsubstituted alkenyl group by hydrogenating the carbon-carbon double bond of the alkenyl group. As the method of hydrogenation, a catalytic hydrogenation method using hydrogen in the presence of a hydrogenation catalyst can be given. There are no specific limitations to the hydrogenation catalyst. For example, a palladium catalyst such as palladium-carbon, Lindler catalyst (palladium-calcium carbonate was poisoned by lead (II) acetate), and palladium-alumina; platinum catalysts such as platinum oxide; ruthenium catalysts such as ruthenium-carbon; and the like can be given. In the hydrogenation reaction, common catalytic hydrogenation conditions can be used without any specific limitations.

【0057】

(3) Optical resolution agent

In the third place, the present invention provides an optical resolution agent comprising at least one 2-oxabicyclo [3.3.0]octane compound of the formula (1).

Although the optical resolution agent of the present invention may be a mixture of diastereomers, an optical resolution agent comprising one diastereomer is preferable for simple and efficient optical resolution.

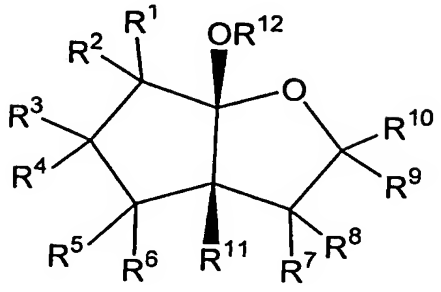
The optical resolution agent of the present invention is useful in the optical resolution of a mixture of optical isomers having an asymmetric carbon atom in the molecule, for example, an alcohol, thiol, carboxylic acid, or sulfonic acid, particularly an optical isomer mixture of alcohol.

【0058】

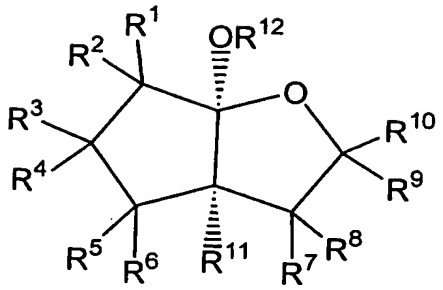
It is known that in the compound having a 2-oxabicyclo[3.3.0]octane skeleton of [a five-member ring + a five-member ring], the position 1 substituent and the position 5 substituent are cis-configured (Tetrahedron Lett., 35, 7785 (1994)). Therefore, if R^1 =R^2, R^3=R^4, R^5=R^6, R^7=R^8, and R^9=R^{10} and R^{12} is an optically active group in the compound of the formula (1), that compound is a mixture of two diastereomers shown in the following formulas (1a) and (1b).

【0059】

【Chemical formula 10】



(1a)



(1b)

【0060】

The mixture of the diastereomer of the formula (1a) and the diastereomer of the formula (1b) can be isolated into individual diastereomers by a separation means such as column chromatography, simulated moving bed chromatography, distillation, or crystallization.

【0061】

Hereinafter, method for optical resolution of optical isomer mixture of alcohol using an optical resolution agent of the present invention will be described by giving an example of a compound of the formula (1a), wherein all of $R^1 \sim R^{10}$ are hydrogen atom, as an optical resolution agent.

【0062】

The compound of the formula (1c) as shown below can be obtained by reaction of one of the diastreomer (1a) which is separated from the diastereomer mixture with lower alcohol of the formula R^{13}-OH (wherein R^{13} represents a lower alkyl group such as methyl group, ethyl group etc.) in the presence of acid catalyst.

The compound of the formula (1c) is an optically active substance having a steric configuration, in which the position 1 substituent (R^{11}) and the position 5 substituent (OR^{13}) on the 2-oxabicyclo[3.3.0]octane ring are cis-configured with each other, with either substituent being on the α-plane with respect to the other.

The reason why the diastreomer (1a) is converted to the compound of the formula (1c) is to make easy removing alcohol of the formula R^{13}-OH from the reaction mixture.

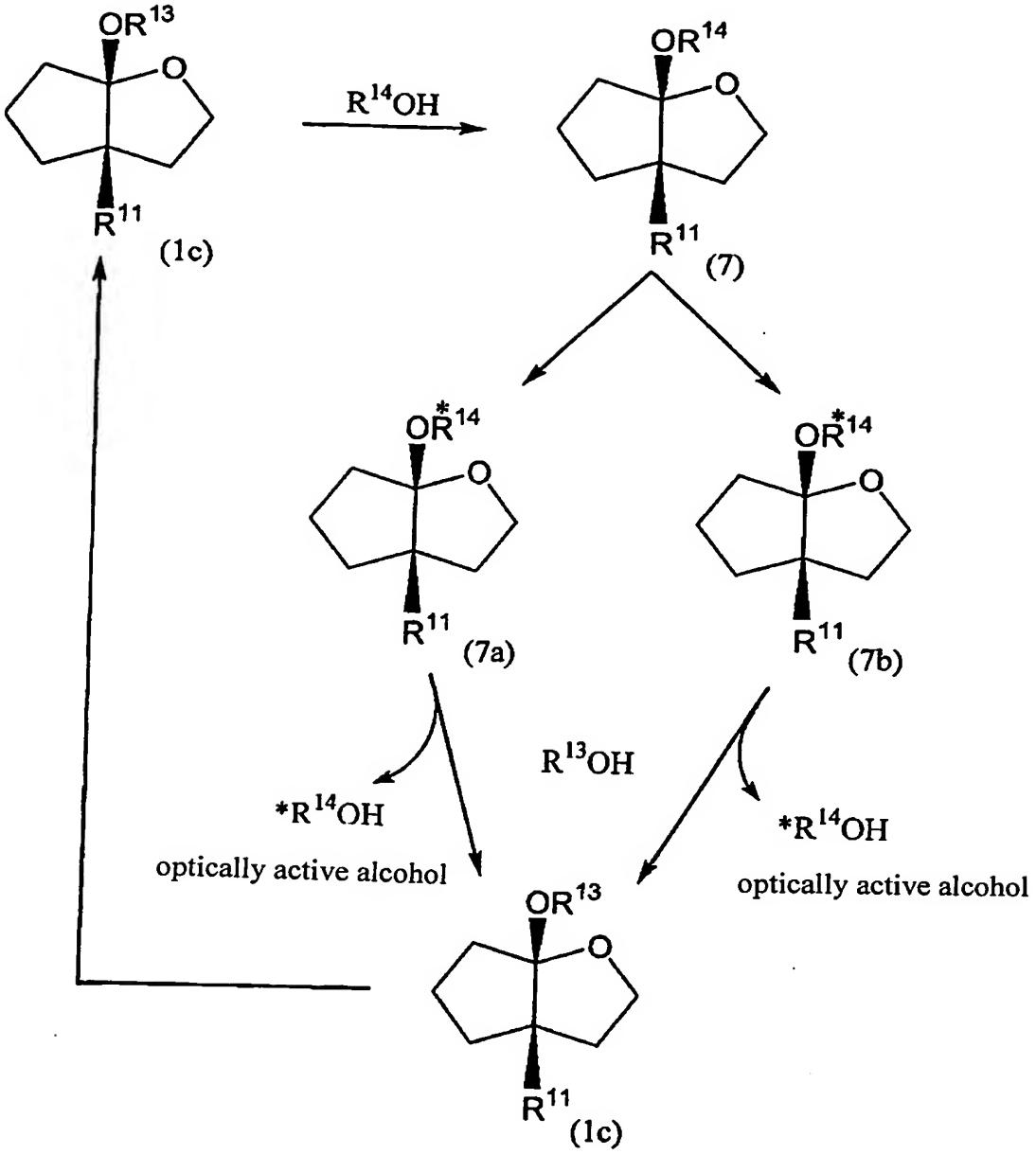
Of course, this step may be optionally omitted, in which case the compound of the above formula (1a)(or (1b)) can be used as an optical resolution agent as is.

【0063】

The outline of the method for optical resolution of optical isomer mixture of alcohol represented by the formula R^{14}-OH using a kind of diastreomer (the compound represented by the formula(1c)) is shown below.

【0064】

【Chemical formula 11】



【0065】

In the formula, * represents a chiral (optically active) group.

For the first, the compound of the formula (1c) is reacted with an optical isomer mixture of an alcohol of the formula $R^{14}OH$ in the presence of an acid catalyst to obtain a diastereomer mixture (7). The same reaction conditions and acid catalysts as described in connection with process for the production of 2-oxabicyclo [3.3.0]octane compound (1)

can be used.

The alcohol represented by the formula $R^{14}OH$ is not limited inasmuch as the optical isomer mixture of an alcohol has an asymmetric carbon atom in the molecule. Any alcohol among primary alcohols, secondary alcohols, and tertiary alcohols can be used.

【0066】

Next, the resulting diastereomer mixture (7) is separated into individual diastereomers ((7a),(7b)) by separating methods such as common column chromatography, simulated moving bed chromatography, distillation, and crystallization and the like.

【0067】

Next, the separated diastereomer (7a) is reacted with an alcohol of the formula $R^{13}OH$, wherein R^{13} is the same as defined above, in the presence of an acid catalyst to obtain an optically active alcohol of the formula $R^{14}OH$ and compound of the formula(1c).

Similarly, the other diasteremer (7b) is reacted with an alcohol of the formula $R^{13}OH$, wherein R^{13} is the same as defined above, in the presence of an acid catalyst to obtain the other optically active alcohol of the formula $R^{14}OH$ and compound of the formula(1c).

【0068】

The resulting optical active alcohol of the formula R^{14}-OH can be isolated from the reaction solution by a known purification-separation means such as distillation, column chromatography, and the like.

And the compound of the formula (1c) can be reused as an optical resolution agent after purification if necessary.

【0069】

【Examples】

The present invention will now be described in detail by way of examples, which should not be construed as limiting the present invention. In the examples below "parts" indicates "parts by weight", unless otherwise specified.

【0070】

Preparation Example 1

Preparation of 2-(2-acetoxyethyl)cyclopentanone

2-(2-Acetoxyethyl)cyclopentanone which is a starting raw material for the preparation of 1-methoxy-2-oxabicyclo[3.3.0]octane was synthesized as described in Tetrahedron Lett., 35, 7785 (1994).

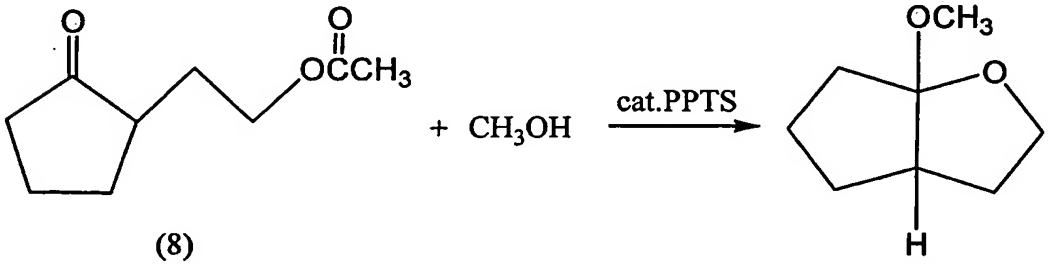
【0071】

Example 1

Preparation of 1-methoxy-2-oxabicyclo[3.3.0]octane (9)

【0072】

【Chemical formula 12】



(8) (9)

【0073】

A reaction vessel was charged with 21 parts of anhydrous toluene, 0.6 parts of methanol, 0.2 part of pyridinium paratoluene sulfonate (PPTS), 2.0 parts of 2-(2-acetoxyethyl)cyclopentanone (8) obtained in Preparation Example 1 at room temperature. The mixture was refluxed for seven hours with stirring. After the reaction, the reaction mixture was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (n-hexane : ethyl

acetate = 19 : 1) to obtain 1.6 parts of 1-methoxy-2-oxabicyclo[3.3.0]octane (9) (yield: 95%).

【0074】

<Properties of Compound (9)>

EI-MS: m/z 158 (M^+)

^{13}C-NMR ($CDCl_3$, δ ppm); 24.13, 31.63, 33.79, 34, 86. 47.78, 50.40, 67.86, 120.33

^{1}H-NMR ($CDCl_3$, δ ppm); 1.3-2.5 (m, 9H), 3.20 (s, 3H), 3.72 (dddd,1H), 3.86 (dddd, 1H)

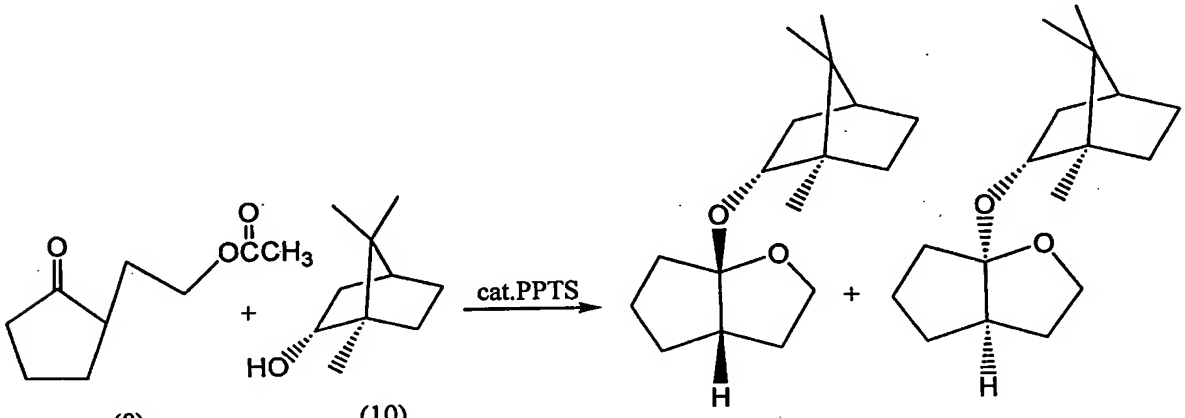
【0075】

Example 2

Preparation of 5-[((1S)-endo) -(-)-bornyloxy]-2-oxabicyclo [3.3.0]octane (11a, 11b)

【0076】

【Chemical formula 13】



(8) (10) (11a) (11b)

【0077】

A reaction vessel was charged with 20 parts of 2-(2-acetoxyethyl)cyclopentanone (8) obtained by Preparation Example 1, 2 parts of pyridinium paratoluene sulfonate (PPTS), 18 parts of ((1S)-endo)-(-)-borneol (10), and 200 parts of anhydrous toluene at room temperature. The mixture was refluxed for five

hours with stirring. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (n-hexane : diethyl ether = 40 : 1) to obtain 14.7 parts of the target isomer mixture (yield 95%).

【0078】

The diastereomer mixture obtained was separated into individual diastereomers (11a and 11b) by silica gel column chromatography (n-hexane : diisopropyl ether = 1 : 40).

The properties of the two diastereomers (Isomer 1 and Isomer 2) represented respectively by the formulas (11a) and (11b) are shown below. Among the isomers separated by the silica gel column chromatography, the isomer having a larger Rf value is indicated as Isomer 1 and the isomer having a smaller Rf value is indicated as Isomer 2.

【0079】

<Properties of Isomer 1>

EI-MS: m/z 264 (M^+)

^{13}C-NMR ($CDCl_3$, δ ppm); 13.56, 19.00, 19.92, 24.36, 26.72, 28.46, 31.77, 34.19, 36.57, 38.64, 45.46, 47.14, 47.99, 49.09, 67.44, 77.96, 119.96

^{1}H-NMR ($CDCl_3$, δ ppm); 0.70-0.84 (sss, 9H), 0.90-2.48 (m, 16H), 3.68-3.96 (m,3H)

Optical rotation: $[\alpha]_D^{23}$ = -67.38° (c = 1.523, $CHCl_3$)

【0080】

<Properties of Isomer 2>

EI-MS: m/z 264 (M^+)

^{13}C-NMR ($CDCl_3$, δ ppm); 13.78, 18.92, 19.92, 24.27, 26.69, 28.46, 31.67, 34.36, 36.19, 38.87, 45.24, 47.07, 48.37, 48.84, 67.81, 79.17, 120.82

^{1}H-NMR ($CDCl_3$, δ ppm); 0.70-0.84 (sss, 9H), 0.90-2.48 (m, 16H), 3.68-3.96 (m,3H)

Optical rotation: $[\alpha]_D^{23} = -1.36°$ (c = 0.525, $CHCl_3$)

【0081】

Preparation Example 2

Preparation of 2-(2-acetoxyethyl)-2-methoxycarbonylcyclopentanone

2-(2-Acetoxyethyl)-2-methoxycarbonylcyclopentanone (12) was prepared by reacting 2-methoxycarbonylcyclopentanone and 2-iodo ethyl acetate in acetone in the presence of potassium carbonate according to the method described in Tetrahedron Lett., 35, 7785 (1994).

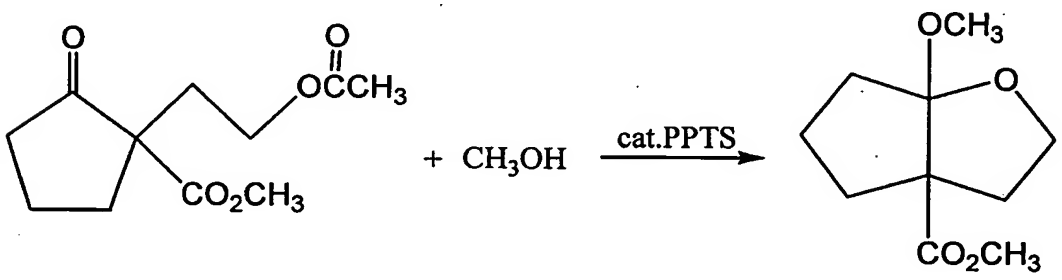
【0082】

Example 3

Preparation of 1-methoxy-5-methoxycarbonyl-2-oxabicyclo[3.3.0]octane (13)

【0083】

【Chemical formula 14】



(12) (13)

【0084】

A reaction vessel was charged with 1,580 parts of methanol, 25 parts of PPTS, 228 parts of 2-(2-acetoxyethyl)-2-methoxycarbonylcyclopentanone (12) obtained in Preparation Example 2 at room temperature. The mixture was refluxed for three hours with stirring. After cooling the reaction solution to room temperature, 30 parts of potassium carbonate was added and the mixture was stirred for one hour at room temperature. Insoluble matters were removed by filtration, the filtrate was washed with a

brine, and the solvent was evaporated. The residue was distilled under reduced pressure to obtain 167 parts of the target compound (13) (yield: 85%). Boiling point: 68°C/3.5 mmHg

【0085】

<Properties of Compound (13)>

EI-MS: m/z 200(M^+)

^{13}C-NMR ($CDCl_3$, δ ppm); 22.59, 34.01, 35.71, 37.10, 51.22, 52.04, 62.22, 67.82, 120.33, 174.02

^{1}H-NMR ($CDCl_3$, δ ppm); 1.49-1.89 (m, 5H), 1.96-2.16 (m,1H) m, 2.33-2.48 (m,1H), 2.62-2.78 (m, 1H), 3.2 (s, 3H), 3.64 (s, 3H), 3.82-3.98 (m, 2H)

【0086】

Preparation Example 3

Preparation of 2-(2-acetoxyethyl)-2-(2-propenyloxycarbonyl)cyclopentanone

A four-necked flask equipped with a thermometer and a reflux tube was charged with 49.5 parts of 60% sodium hydride, 254 parts of diallyl carbonate, and 711 parts of tetrahydrofuran under a nitrogen stream. The mixture was heated while refluxing. 100 parts of cyclopentanone dissolved in 445 parts of tetrahydrofuran was dropped for one hour, followed by refluxing for three hours. After evaporating the solvent tetrahydrofuran and the produced allyl alcohol from the resulting mixture, 865 parts of toluene and 103 parts of N-methylpyrrolidone were added, and the mixture was heated to 100°C. Then, 264 parts of 2-iodo ethyl acetate was added dropwise for one hour, followed by stirring for one hour at the same temperature. The reaction mixture was cooled and washed with 3% hydrochloric acid aqueous solution and saturated sodium thiosulfate aqueous solution. The solvent was evaporated and the residue was distilled to obtain 258 parts of the target compound (yield: 86%).

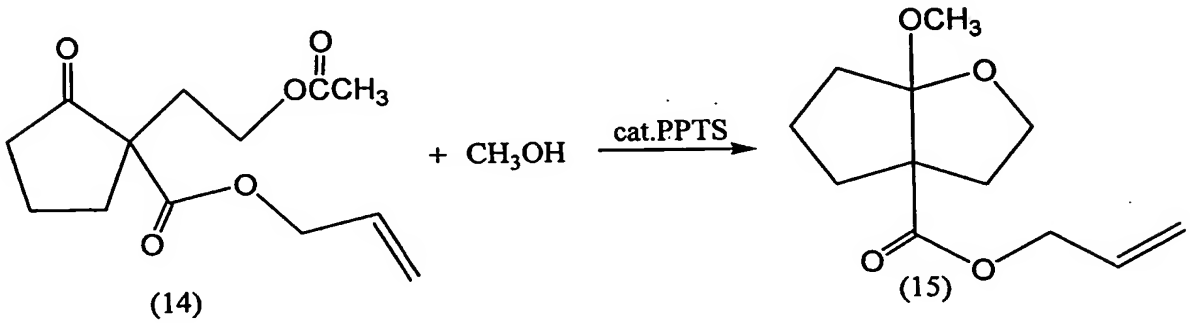
【0087】

Example 4

Preparation of 1-methoxy-5-(2-propenyloxycarbonyl)-2-oxabicyclo[3.3.0]octane (15)

【0088】

【Chemical formula 15】



(14) (15)

【0089】

A reaction vessel was charged with 1,580 parts of methanol, 25 parts of PPTS, 254 parts of 2-(2-acetoxyethyl)-2-(2-propenyloxycarbonyl)cyclopentanone (14) obtained in Preparation Example 3 at room temperature. The mixture was refluxed for three hours with stirring. After cooling the reaction solution to room temperature, 30 parts of potassium carbonate was added and the mixture was stirred for one hour at room temperature. Insoluble matters were removed by filtration, the filtrate was washed with saturated brine, and the solvent was evaporated. The residue was distilled under reduced pressure to obtain 146 parts of the target compound (15) (yield: 80%).

【0090】

Preparation Example 4

Preparation of 1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane

1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane was prepared according to the method described in Tetrahedron Lett., 35, 7785 (1994).

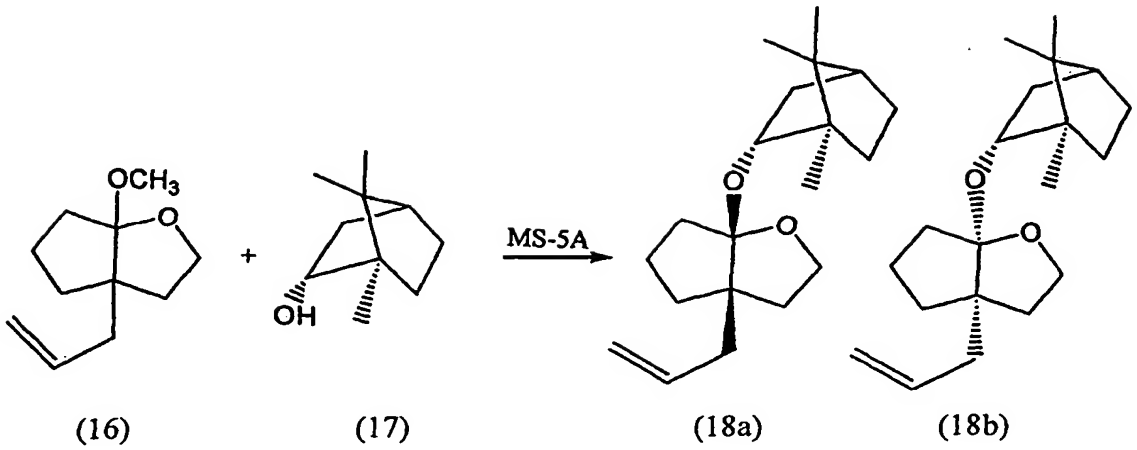
【0091】

PreparationExample 5

Preparation of 1-[((1S)-endo)-(-)-bornyloxy]-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane and separation of diastereomers (18a, 18b)

【0092】

【Chemical formula 16】



(16) (17) (18a) (18b)

【0093】

22.8 parts of ((1S)-endo)-(-)-borneol (17) was added to 35 ml of an anhydrous toluene solution containing 30 parts of 1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane (16) and 30 parts of molecular-sieve 5A at room temperature. The mixture was stirred for 10 hours at 110°C. In this instance, 600 parts of molecular-sieve (MS-4A) that can adsorb methanol was filled in the reflux tube to adsorb the methanol generated in the reflux tube. The reaction solution was filtrated. The filtrate was concentrated under reduced pressure to obtain 52 parts of a residue. The resulting residue was purified by silica gel column chromatography (n-hexane : diethyl ether = 40 : 1) to obtain the target isomer mixture. Furthermore, the resulting isomer mixture was separated into individual diastereomers represented by (18a) and (18b) (Isomer 1 and Isomer 2) by silica gel column chromatography (n-hexane : diisopropyl ether = 1 : 40). Isomer 1 (diastereomer having a larger Rf) and Isomer 2 (diastereomer having a smaller Rf) were obtained respectively in an amount of 17.1 parts (yield: 38%) and 18.9 parts (yield: 42%).

【0094】

The properties of the diastereomers represented by (18a and 18b) are shown as follows.

<Properties of Isomer 1>

Rf (Rf value when developed using n-hexane : toluene = 2 : 1 for a length of 44 mm)

Rf = 0.36

EI-MS: m/z 304 (M^+)

FT-IR (nujor): 3180, 2960, 2880, 1645, 1480, 1460, 1400, 1375, 1330, 1310, 1240, 1195, 1125, 1060, 1025, 960, 948, 920cm^{-1}

^{1}H-NMR ($CDCl_3$, δ ppm): 0.80 (s, 3H), 0.84 (s, 6H), 0.95-2.22 (m, 16H), 2.27 (m, 1H), 3.98-4.10 (m, 1H), 3.70-3.92 (m, 2H), 5.04-5.09 (m, 2H), 5.88 (ddd, J = 7.0, 10.0, 16.5Hz, 1H),

Optical rotation: $[\alpha]_D^{25}$ = -74.18° (c = 1.05, $CHCl_3$)

【0095】

<Properties of Isomer 2>

Rf (Rf value when developed using n-hexane : toluene = 2 : 1 for a length of 44 mm)

Rf = 0.28

EI-MS: m/z 304 (M^+)

FT-IR (nujor): 3180, 2960, 2880, 1645, 1478, 1460, 1395, 1375, 1325, 1310, 1240, 1195, 1120, 1058, 1025, 960, 948, 920cm^{-1}

^{1}H-NMR ($CDCl_3$, δ ppm): 0.80 (s, 3H), 0.84 (s, 6H), 0.95-2.22 (m, 16H), 2.27 (m, 1H), 3.70-3.92 (m, 3H), 5.04-5.09 (m, 2H), 5.88 (ddd, J = 7.0, 10.0, 16.5Hz, 1H),

Optical rotation: $[\alpha]_D^{25}$ = +5.56° (c = 0.84, $CHCl_3$)

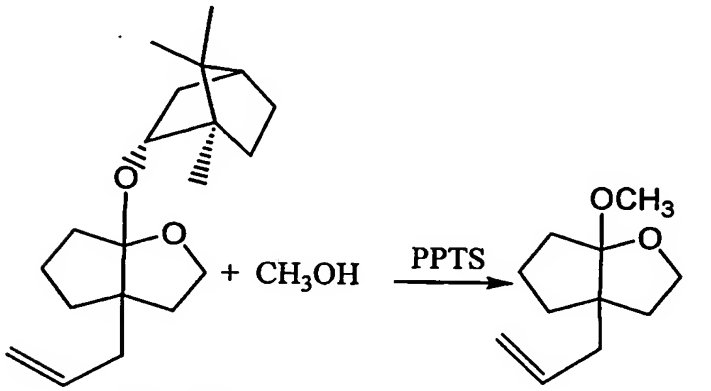
【0096】

Preparation Example 6

Preparation of 1-methoxy-5-(-propenyl)-2-oxabicyclo[3.3.0]octane (16a, 16b)

【0097】

【Chemical formula 17】



(18a,18b) (16a,16b)

【0098】

Methanol and PPTS were added to a methylene chloride solution of the diastereomer of 1-[((1S)-endo)-(-)-bornyloxy]-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane (Isomer 1) obtained in preparation Example 5 respectively in an amount of 0.9 mol and 0.1 mol per one mol of the 1-[((1S)-endo)-(-)-bornyloxy]-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane. The mixture was stirred at room temperature for 30 minutes. The reaction solution was washed with saturated brine, dried over anhydrous potassium carbonate, and filtered. The filtrate was concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography (n-hexane : ethyl acetate = 19 : 1) to obtain the target diastereomer of 1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane (Isomer 3).

【0099】

The same reaction was carried out using a diastereomer of 1-[((1S)-endo)-(-)-bornyloxy]-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane (Isomer 2) to obtain another diastereomer of 1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane (Isomer 4).

【0100】

The structures of the diastereomers (Isomer 3 and Isomer 4) of 1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane shown by the formulas (16a) and (16b) were confirmed by measuring FT-IR, ^{1}H-NMR, ^{13}C-NMR, and EI-MS spectrum.

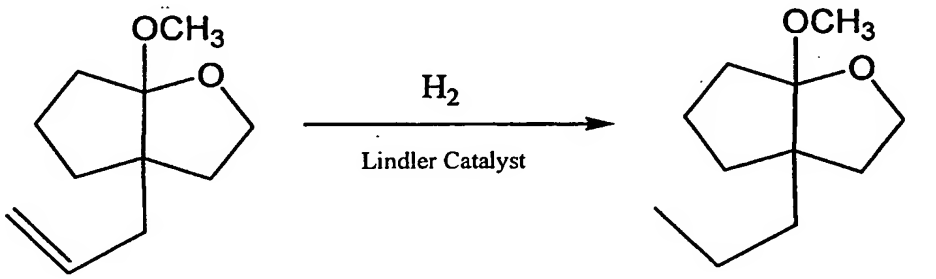
【0101】

Example 5

Preparation of 1-methoxy-5-n-propyl-2-oxabicyclo[3.3.0]octane (20a, 20b)

【0102】

【Chemical formula 18】



(16a,16b) (20a,20b)

【0103】

0.01 part of Lindler catalyst (manufactured by Aldrich Co.) was added to a solution of 0.2 part of a diastereomer (Isomer 3) of 1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane obtained in Preparation Example 6 in 8 parts of methanol. The hydrogenation reaction was carried out at room temperature in a nitrogen atmosphere under a small hydrogen pressure for two hours. After the reaction, the catalyst was removed by filtration and the filtrate was concentrated under reduced pressure to obtain 0.2 part of one diastreomer (Isomer 5) of the target 1-methoxy-5-n-propyl-2-oxabicyclo[3.3.0]octane as a colorless oil (yield: 96%).

【0104】

The same reaction was carried out using another diastereomer (Isomer 4) of 1-methoxy-5-(2-propenyl)-2-oxabicyclo[3.3.0]octane obtained in Preparation Example 6

to obtain another diastreomer (Isomer 6) of the target 1-methoxy-5-n-propyl-2-oxabicyclo[3.3.0]octane (yield: 95%).

The properties of the two diastereomers (Isomer 5 and Isomer 6) respectively represented by the formulas (20a) and (20b) are as follows.

【0105】

<Properties of Isomer 5> 1-methoxy-5-n-propyl-2-oxabicyclo[3.3.0]octane

EI-MS: m/z 184 (M^+)

^{1}H-NMR ($CDCl_3$, δ ppm); 0.90-0.95 (m, 3H), 1.20-1.67 (m, 9H), 1.67-1.75 (m, 1H), 1.84-1.92 (m, 1H), 2.02-2.10 (m, 1H), 3.30 (s, 3H), 3.77-3.84 (m, 2H)

Optical rotaion: $[\alpha]_D^{25} = -47.88°$ (c = 0.943, $CHCl_3$)

【0106】

<Properties of Isomer 6> 1-methoxy-5-n-propyl-2-oxabicyclo[3.3.0]octane

EI-MS: m/z 184 (M^+)

^{1}H-NMR ($CDCl_3$, δ ppm); 0.88-0.98 (m,3H), 1.20-1.67 (m, 9H), 1.67-1.76 (m, 1H), 1.83-1.92 (m, 1H), 2.02-2.11 (m, 1H), 3.30 (s, 3H), 3.77-3.84 (m, 2H)

Optical rotaion: $[\alpha]_D^{25} = +38.81°$ (c = 0.696, $CHCl_3$)

【0107】

【Effect of the Invention】

According to the present invention, an optical isomer mixture of a compound such as alcohol can be optically resolved using a simple method and a novel 2-oxabicyclo[3.3.0]octane compound which can be used as an optical resolution agent with high versatility can be provided.

According to the present invention, the 2-oxabicyclo[3.3.0]octane compound of the present invention can be produced in a high yield using a simple process of reacting an easily available cyclopentanone compound with an alcoholic compound.

【Name of Document】 ABSTRACT

【Abstract】

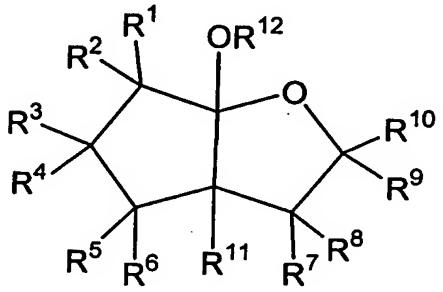
【Object】

To provide a novel 2-oxabicyclo[3.3.0]octane compound which can be used as an optical resolution agent of an optical isomer mixture of alcohol etc., a process for producing such a compound, and an optical resolution agent containing at least one 2-oxabicyclo[3.3.0]octane compound.

【Means for Settlement】

2-Oxabicyclo[3.3.0]octane compounds represented by the following formula (1) ; a process for producing the compounds (1); and an optical resolution agent comprising at least one of the compounds (1).

【Chemical formula 1】,



(1)

wherein R^1-R^{10} individually represent a hydrogen atom or an alkyl group having 1-20 carbon atoms, R^{11} represents a hydrogen atom, a substituted or unsubstituted alkoxycarbonyl group etc., and R^{12} represents a substituted or unsubstituted hydrocarbon group.

【Chosen Drawing】 None